Remarks

Applicants have canceled claims 90-136 without prejudice and added claims 137-206. Further, Applicants have amended the specification to update the status of a priority document and submitted an amended sequence listing. Attached hereto is a marked-up version of the changes made to the specification by the current amendment, captioned "Version With Markings To Show Changes Made." The amendment is fully supported by the specification and claims as originally filed, and thus no new matter has been added.

Claims 137-206 will be pending will be pending upon entry of these amendments. Applicants respectfully request reconsideration of the rejections and objections in view of the following remarks.

I. Amendment of the Specification.

The specification has been amended to update the status of a priority document. More particularly, at page 1 after the title, the patent number and issue date of U.S. Application No. 08/483,534 has been added. Further, the sequence listing has been amended to correct errors in SEQ ID NO:7. In particular, residues 93 and 135 have been corrected to read as "L," and residue 161 has been corrected to read as "G." These amendments are fully supported by the specification and claims as originally filed. More particularly, support for the amendments to SEQ ID NO:7 can be found in Figure 2 as originally filed. Accordingly, no new matter has been added by way of amendment, and entry of the above amendments is respectfully solicited.

II. Amendment of the Claims.

Claims 90-136 have been canceled in favor of new claims 137-206 in order to cover additional embodiments of the subject matter of the elected group. Applicants submit that the subject matter of new claims 137-206 falls within the scope of Group I, as defined by the Examiner in the Office Action mailed May 14, 1998 (Paper No. 3).

New claims 137-206 find support in the claims as originally filed and throughout the specification. Specifically, support for new claims 137-206 is found, for example, at page 4, first full paragraph through page 5, first full paragraph; at page 8, first and second full paragraphs; at page 7, first and second full paragraphs; at the paragraph bridging pages 6 and 7; at page 7, second full paragraph; at the paragraph bridging pages 8 and 9; at page 12, second full paragraph; at page 13, first full paragraph; at page 15, second full paragraph; and at the paragraph bridging pages 16 and 17.

Accordingly, no new matter has been added by way of amendment, and entry of the above amendment is respectfully solicited.

III. Applicants' Request to Have an Interference Declared Between the Instant Application and U.S. Patent No. 6,090,377.

Pursuant to 37 C.F.R. §1.607, Applicants respectfully request that an interference be declared between U.S. Serial No. 08/972,301 and U.S. Patent 6,090,377, issued July 18, 2000 ("the '377 Patent", attached hereto as reference DB). Applicants have become aware of the '377 Patent, which discloses and claims a polypeptide identical to the polypeptide shown as SEQ ID NO:2 in the present application. New claims 203 to 206 are patentable over the prior art and define the same invention as claims 1 and 2 of the '377 Patent. New claims 203 to 206 are submitted for the purpose of provoking Interference proceedings.

They are presented as a proposed count. Claims 1 and 2 of the '377 Patent correspond to the proposed count. Applicants respectfully point out that U.S. Application No. 08/705,868, to which the '377 Patent claims priority, was filed on August 28, 1996, over one year and two months later than the June 7, 1995 filing date of U.S. Application No. 08/483,534 (now U.S. Patent No. 6,013,483, issued on January 11, 2000), to which the instant application, U.S. Application No. 08/972,301, claims priority.

The pertinent facts required under 37 C.F.R. § 1.607 are as follows:

Identification of the patent (37 C.F.R. § 1.607 (a)(1))

U.S. Patent 6,090,377

Presentation of the proposed count (37 C.F.R. § 1.607 (a)(2))

The proposed count corresponds to new claims 203 to 206:

203. (New) A substantially purified polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO:2.

204. (New) A substantially purified polypeptide comprising the amino acid sequence of SEQ ID NO:2.

205. (New) A pharmaceutical composition comprising at least a portion of the amino acid sequence of SEQ ID NO:2 and a pharmaceutically acceptable excipient.

206. (New) A pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:2 and a pharmaceutically acceptable excipient.

Identification of at least one claim in the patent corresponding to the proposed count (37 C.F.R. § 1.607 (a)(3))

Claims 1 and 2 of U.S. Patent 6,090,377

Presentation of at least one claim corresponding to the proposed count . . . and, if any claim of the patent or application identified as corresponding to the proposed count does not correspond exactly to the proposed count, an explanation of why each such claim corresponds to the proposed count. (37 C.F.R. § 1.607 (a)(4))

Amended claims 203 to 206 of the instant application correspond exactly to the proposed count. Claims 1 and 2 of the '377 Patent correspond substantially to the proposed count, as they claim "at least a portion of SEQ ID NO:1" of the '377 Patent. Applicants respectfully point out that residues 1 to 168 of SEQ ID NO:2 of the instant application are identical to residues 134 to 301 of SEQ ID NO:1 of the '377 Patent. Because residues 134 to 301 of SEQ ID NO:1 of the '377 Patent comprise "at least a portion of SEQ ID NO:1," claims 1 and 2 of the '377 Patent correspond to the proposed count.

Application of the terms of any application claim: (i) identified as corresponding to the count, and (ii) not previously identified in the disclosure of the application. (37 C.F.R. § 1.607 (a)(5))

The terms of the instant application claims that correspond to the count are present in the disclosure of the application. More particularly, support for the term "substantially purified" can be found, for example, at page 9, first and second full paragraphs; and at page 15, first and second full paragraphs. Support for the term "polypeptide" can be found, for example, at page 2, first and second full paragraphs; at page 3, last paragraph, to page 4, first paragraph; and at page 8, first to third full paragraphs. Support for the term "portion" can be found, for example, at page 7, second full paragraph; and at page 8, first

to third full paragraphs. Support for the term "amino acid sequence of SEQ ID NO:2" can be found, for example, at page 4, second full paragraph; at page 5, third full paragraph; at page 8, first and second full paragraphs; in the Sequence Listing at SEQ ID NO:2; and in Figure 1. Support for the term "pharmaceutical composition" can be found, for example, at page 16, last paragraph, to page 17, second full paragraph. Support for the term "pharmaceutically acceptable excipient" can be found, for example, at page 16, last paragraph, to page 17, second full paragraph.

IV. Rejection of the Claims under 35 U.S.C. §§ 101 and 112, First Paragraph.

The Examiner has rejected claims 90-136 under 35 U.S.C. § 101 because the invention is allegedly not supported by either a specific and substantial asserted utility or a well established utility. (*See* Paper No. 21, Pages 2-4.) The Examiner contends that "the assertion that EMAP III has similar biological activities as EMAP II cannot be accepted in the absence of supporting evidence." The Examiner has further rejected claims 90-136 under 35 U.S.C. § 112, first paragraph, because one skilled in the art would allegedly not know how to use the claimed invention so that it would operate as intended without undue experimentation, based on the supposed lack of either an specific and substantial asserted utility or a well established utility. Applicants have canceled claims 90-136, thereby obviating any rejection of these claims. However, Applicants respond to the rejections as it may be held to apply to new claims 137-206.

Applicants respectfully disagree and traverse these rejections.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the applicant in the written description of the invention. *See* M.P.E.P.

§§ 2107.01(II) – (III) (7th Ed. Rev. 1, Feb. 2000). In addition, an applicant need only make *one* credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101. *See, e.g., Raytheon v. Roper,* 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."); *see also* M.P.E.P. § 2107.01 at 2100-29; Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (January 5, 2001). Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. *See* M.P.E.P. § 2107.01(II)(B); Utility Examination Guidelines at 1098.

Moreover, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt *(i.e.,* "question") the truth of the statement of utility. *See* M.P.E.P. § 2107.01(II)(A); Utility Examination Guidelines at 1098-99. Thus, the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. *See id.* The Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. *See id.*; *see also In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, the Examiner has not met the burden that is necessary to establish and maintain a rejection for lack of utility under 35 U.S.C. § 101.

As the Examiner recognized in the Office Action at page 3, the specification points out that Endothelial Monocyte Activating Polypeptide III ("EMAP III") should have similar biological activities to EMAP II. *See, e.g.,* Specification at page 2, lines 13-15, at page 4, lines 15-17, and at Figure 2. Based on such asserted activities, and contrary to the Examiner's comments, the specification provides guidance to the skilled artisan to use the

polypeptides of the present invention for similar purposes as EMAP II, including but not limited to: activating endothelial and mononuclear cells; potentiating the participation of endothelial and mononuclear cells in procoagulant reactions through induction of tissue factor; promoting migration of mononuclear phagocytes and polymorphonuclear leukocytes; stimulating the production of tumor necrosis factor-α and tissue factor by mononuclear phagocytes; stimulating the release of myeloperoxidase by polymorphonuclear leukocytes; elevating cytosolic free calcium concentration, peroxidase generation, and chemotaxis; releasing von Willebrand factor; stimulating expression of the adhesion molecules E-selectin and P-selectin; leading to a phlogogenic response when injected into murine foot pads; and inducing acute thrombohemorrhage and partial tumor regression in Meth A sarcomas. *See id*; Kao *et al., J. Biol. Chem.* 269:25106-19 (1994); Wakasugi *et al.*, "Two distinct cytokines released from a human aminoacyl-tRNA synthetase," *Science* (1999) April 2; 284:147-51 (submitted herewith as Reference DC). Applicants assert that such characterization of the invention is sufficient to constitute a showing of utility.

In arguing that Applicants' asserted utility is not credible, the Examiner must attack (a) the logic underlying the assertion as seriously flawed or (b) the facts upon which the assertion is based as inconsistent with the logic underlying the assertion. *See, e.g.*, Revised Interim Utility Guidelines Training Materials, p. 5. In the instant rejection, the Examiner merely argues that "the specification fails to support a specific and substantial utility for EMAP III," apparently based on the Examiner's earlier contention that "the assertion that EMAP III has similar biological activities as EMAP II cannot be accepted in the absence of supporting evidence." Applicants point out that the Utility Examination Guidelines require an evaluation of the utilities taught in the closest prior art, in the instant

case, EMAP II. *See* Utility Examination Guidelines at 1098. Thus, Applicants assert that the Examiner has not satisfied her burden to make a *prima facie* showing that Applicants' asserted utility is not credible.

Applicants submit herewith Wilson *et al.*, "Assessing Annotation Transfer for Genomics: Quantifying the relations between protein sequence, structure, and function through traditional and probabilistic scores," *J. Mol. Biol.* (2000) Mar 17; 297(1):233-49 (submitted herewith as Reference DD). In this publication, the authors report distinct thresholds for sequence, structure, and function: at least 40% sequence identity corresponds to a sharing of precise function while sequence identities of about 25% comprise a functional class. Figure 7A of Wilson *et al.* demonstrates that two proteins sharing 20% sequence identity have a greater than 70% chance of being a member of the same functional class. Likewise, Pawlowski *et al.* (submitted herewith as Reference DE) report that polypeptide sequence identities of even less than 25% may be used to predict function with above random probability. The authors teach "[i]t is very encouraging, that even below this threshold [*i.e.*, 25% identity], the sequence similarity can be recognized and function similarity can be predicted with above random probability." *See* Pawlowski et al., 2000 Pacific Symposium on BioComputing, p. 6. Applicants assert that these papers confirm Applicants' contention that, based on identity data, it is "more likely than not" that one skilled in the art would consider Applicants' asserted utility to be credible. *See*, M.P.E.P 706.03(a)(1)(C)(1), pp. 700-30.

Applicants further submit Wakasugi *et al.* (Reference DC). Applicants point out that the "COOH- terminal domain of human TyrRS" referred to in Wakasugi *et al.* has the exact amino acid sequence of SEQ ID NO:2 of the present invention. *Compare* Kleeman *et al.*, "Human tyrosyl-tRNA synthetase shares amino acid sequence homology with a

putative cytokine," *J. Biol. Chem.* (1997) May 20; 272(22):14420-25 (Reference C4, submitted December 3, 1999) *with* SEQ ID NO:2. Wakasugi *et al.* report at page 147 that:

> The COOH-terminal domain induced migration of human MPs from peripheral blood to an extent comparable to that seen with mature human EMAP II (Fig. 2A)... The COOH-terminal domain of TyrRS also stimulated TNFα and MP tissue factor activities (Fig. 2, A and B), induced release of PMN myeloperoxidase activity in the peroxidase generation assay (Fig. 2B), and induced PMN migration in chemotaxis chambers (Fig. 2C). The induction of PMN migration by the COOH-terminal domain and mature EMAP II showed the bell-shaped concentration dependence that is characteristic of chemotactic cytokines.

Wakasugi *et al.* further report at page 151 that human TyrRS is secreted from apoptotic cells, as is human EMAP II.

Applicants assert that the only reasonable conclusion that could be reached based on Wakasugi *et al.*, and the fact that the statements made by Examiner are unsupported by evidence to the contrary, is that the EMAP III polypeptides of the present invention have similar biological activities to EMAP II. Thus, Applicants have shown that EMAP III has both significant identity and similar biological activities to EMAP II. Accordingly, even assuming *arguendo* that the Examiner has made a *prima facie* showing that Applicants' asserted utility is not credible, Applicants respectfully submit that the *prima facie* showing has been rebutted, and that the presently claimed invention possesses credible, well-established utilities which constitute patentable utilities under 35 U.S.C. § 101.

In addition to the biological activity of EMAP III, Applicants have contemplated and disclosed therapeutic applications of EMAP III, for example, regression of neoplasia (such as tumors in cancer), consistent with the biological activity of EMAP III. *See* Specification at page 15, third full paragraph. Applicants submit that this asserted utility for EMAP III is specific (not every protein may be used to regress neoplasia) and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet

the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). In addition, Applicants submit that this utility is credible, especially in light of the data presented by Wakasugi *et al.* Moreover, the Examiner has failed to provide any countervailing statements as to why this particular utility is not specific, substantial and credible.

In regard to this asserted therapeutic activity, Applicants note that there is no need to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty or provide actual evidence of success in treating humans where such a utility is asserted. M.P.E.P. § 2107.02 (I) at 2100-33 to 2100-34. All that is required of Applicants is that there be a reasonable correlation between the biological activity and the asserted utility. *See Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980). Moreover, "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, *necessarily* includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana,* 51 F.3d 1560, 1568 (Fed. Cir. 1995) (emphasis added).

Even assuming *arguendo* that the Examiner has established a *prima facie* showing that the claimed invention lacks utility, Applicants respectfully submit that they have rebutted the Examiner's showing by proffering sufficient evidence to lead one skilled in the art to conclude that the asserted utilities are more likely than not true. Applicants have also directed the Examiner to the specification where clear and specific assertions are made of EMAP III polypeptide biological and therapeutic activity.

In view of the above, Applicants respectfully submit that the presently claimed invention possesses credible, well-established utilities which constitute patentable utilities

under 35 U.S.C. § 101. Because Applicants' assertions of utility are sufficient to satisfy the requirements of 35 U.S.C. § 101, it is respectfully requested that the Examiner's rejection of the claims under 35 U.S.C. § 101 be reconsidered and withdrawn.

Further, the Federal Circuit and its predecessor determined that the utility requirement of 35 U.S.C. § 101 and the how to use requirement of 35 U.S.C. § 112, first paragraph, have the same basis, *i.e.*, the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); *see also* M.P.E.P. § 2107(IV); Utility Examination Guidelines at 1098. As discussed above, the specification teaches specific and well-established utilities of the claimed invention, thereby enabling the skilled artisan to use the claimed polypeptides. Since the specification teaches how to use the claimed polypeptides with only routine experimentation and the specification describes specific and immediate utilities for the claimed polypeptides, Applicants submit that the full scope of the claims is enabled. Accordingly, it is respectfully requested that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

V. Rejections of the Claims under 35 U.S.C. §112, First Paragraph.

A. Polypeptide Variants

Applicants note that although the Examiner did not recite specific claims to which this rejection applies, the Examiner apparently intended to reject claims to polypeptide variants "which are not 100% identical to the polypeptide of SEQ ID NO:2" under 35 U.S.C. § 112, first paragraph. (*See* Paper No. 21, Pages 4-7). The Examiner contends that "Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO:2, but which

still retain a desired property of the polypeptide of SEQ ID NO:2." (Paper No. 21, Page 4). Applicants have canceled claims 90-136, thereby obviating any rejection of these claims. Thus, Applicants respond to the rejection as it may be held to apply to new claims 152-170.

Applicants respectfully disagree and traverse this rejection.

Preliminarily, Applicants point out that in order to enable the claimed invention as required by 35 U.S.C. § 112, the specification need only enable a person of ordinary skill in the art to make the claimed polypeptide variants and practice a single use of the claimed polypeptide variants without undue experimentation. *See, e.g.,* M.P.E.P. § 2164.01(c). Thus, Applicants submit that to be fully enabled, the polypeptide variants of the invention do not necessarily have to be biologically active, but need merely have application in a single use, *e.g.*, to generate an antibody to an EMAP III polypeptide, to bind an antibody to an EMAP III polypeptide, or any of the uses discussed above in Section IV.

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *See Fields v. Conover*, 443 F.2d 1386, 1390-91, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art.

In re Wands involved an appeal from the Board of Appeals and Patent Interferences, affirming the examiner, rejecting immunoassay claims on the grounds that making anti-HBsAg antibodies for use in the claimed immunoassay, other than the

deposited antibody, would be "unpredictable and unreliable, so that it would require undue experimentation for one skilled in the art to make the antibodies." *Id.* at 735, 8 U.S.P.Q.2d at 1402. Antibodies other than the one deposited were described only in terms of function and only a general method of making and using them was disclosed in the application. *See id.* The facts showed that IgM antibodies were disfavored because they tended to self-aggregate and precipitate, isolating the correct antibodies required screening hundreds of clones, and the appellant's first four attempts were unsuccessful. *See id.* at 734, 8 U.S.P.Q.2d at 1402. Nevertheless, the Federal Circuit found that the disclosure satisfied the requirements under § 112 first paragraph. The court based its decision on the fact that the invention could be practiced with "readily available starting materials using methods that are well known in the monoclonal antibody art," and because "practitioners of the art are prepared to screen negative hybridomas in order to find one that makes the desired antibody." *See id.* at 736, 8 U.S.P.Q.2d at 1406.

The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *See id.* at 737, 8 U.S.P.Q.2d at 1404. Furthermore, "[t]here is no magical relation between the number of representative examples and the breadth of the claims" with respect to enablement. *In re Borkowski*, 164 U.S.P.Q. 642, 646 (C.C.P.A. 1970). The issue is not whether the specification discloses any or all alterations that can be made in the claimed polypeptides that will not alter their functional activity, but rather whether polypeptides encompassed by the claims have at least a single use, and this use can be confirmed, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. *See In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976):

> To require such a complete disclosure would apparently necessitate a patent with 'thousands of examples' . . . More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments . . .

Thus, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of the experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue:

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all 'experimentation' is 'undue' since the term 'experimentation' implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.

Id. at 219 (emphasis in the original). Applicants submit that in the instant application, since the disclosed or otherwise known methods of making and screening polypeptides (including variants) may be used to make and then determine, without undue experimentation, whether a given polypeptide encompassed by the claims can be used to generate an antibody to an EMAP III polypeptide, bind an antibody to an EMAP III polypeptide, or for any of the uses discussed above in Section IV, the enablement requirement is fully satisfied. *See In re Wands*, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989).

Applicants further submit that the specification provides ample guidance for one of ordinary skill in the art to routinely make and use the claimed polypeptides. In particular, the specification discloses both the nucleotide and polypeptide sequences (SEQ ID NOS: 1 and 2 respectively) of EMAP III. As the Examiner recognized at page 5 of the Office

Action, the specification also teaches art-recognized procedures for producing and screening for active muteins. Further, the specification teaches, *inter alia*, methods for using the EMAP III polypeptides of the invention to generate antibodies to an EMAP III polypeptide. *See, e.g.*, specification at pages 24-25. Thus, antibodies generated according to the methods disclosed in the specification may routinely be applied to determine whether the EMAP III polypeptides (including variants) bind an antibody to the EMAP III polypeptide disclosed in Figures 1 and 2, respectively. The specification also teaches that the EMAP III polypeptides of the invention have diagnostic and therapeutic applications as discussed above in Section IV. Given the foregoing teachings of the specification, it cannot be said that the invention as claimed is not enabled.

Applicants assert that the Examiner has underestimated the high level of skill of the skilled artisan, and has not considered the fact that the invention could be practiced with readily available starting materials using methods that were well known in the art on the priority date of the instant application. Applicants submit that, like the monoclonal antibody art discussed in *In re Wands*, practitioners making EMAP III polypeptide variants are prepared to screen candidate EMAP III polypeptide variants to find polypeptides that can be used to generate an antibody to an EMAP III polypeptide, bind an antibody to an EMAP III polypeptide, or for any of the uses discussed above in Section IV. Applicants further submit that the skilled protein chemist, molecular biologist, or immunologist, enlightened by the teaching of the present specification, is more than capable of routinely generating the claimed polypeptides and determining whether a polypeptide encompassed by the claims can be used to generate an antibody to an EMAP III polypeptide, bind an antibody to an EMAP III polypeptide, or for any of the uses discussed above in Section IV. Thus, based on the disclosure of the present specification and the knowledge of one of

ordinary skill in the art at the time the application was filed, it is clear that one of ordinary skill in the art would have been able to make and use the invention commensurate with the scope of the claims.

Applicants submit that because of (1) the disclosure and characterization in the specification of the nucleic acid and polypeptide sequence corresponding to EMAP III; (2) the availability of routine techniques for generating fragments or variants to a known polypeptide, for generating antibodies against the polypeptide, and for assaying the ability of an antibody to bind a polypeptide; (3) the high level of skill in the field of protein chemistry, molecular biology and immunology; and (4) the direction and guidance provided by the specification, one skilled in the art could routinely generate the claimed polypeptides and determine whether these polypeptides can be used to generate an antibody to an EMAP III polypeptide, to bind an antibody to an EMAP III polypeptide, or for any of the uses discussed above in Section IV.

A patent applicant's specification disclosure which contains a teaching of how to make and use the invention must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *See In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). Applicants submit that the Examiner has provided no evidence to doubt the enablement of the claimed polypeptides, as discussed above. Thus, Applicants submit that the Examiner has not met her burden in explaining why the skilled artisan would not be enabled to practice the claimed invention throughout the entire scope of the claims. Contrary to the Examiner's assertions, experimentation is not undue merely because it would require assaying "multitudes of variants encompassed by the claimed invention." As set forth in *In re Wands*, "[t]he test is not merely quantitative since a considerable amount of experimentation is permissible, if it

is merely routine." 858 F.2d at 737, 8 U.S.P.Q.2d at 1404. The Examiner is reminded again that in *In re Wands*, the Applicant had to screen hundreds of clones to find one that met the limitations of the claims. *See id.* at 736, 8 U.S.P.Q.2d at 1406.

Applicants further note that Wakasugi *et al.*, discussed in Section IV above, provides specific data confirming the activities of EMAP III recited in the specification. Such data are provided as suggested by the Examiner at page 7 of the Office Action.

In view of the foregoing, Applicants submit that the pending claims fully meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn. Further, in the event that the Examiner maintains the rejection of the claims under 35 U.S.C. § 112, first paragraph, Applicants respectfully request that the Examiner note what subject matter is enabled, as well as any limitations that would render additional subject matter enabled. *See* M.P.E.P. § 2164.04 at page 2100-133; § 2164.08 at page 2100-141.

B. ATCC Deposit Number

The Examiner has rejected claims 96-105 and 123-136 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. In particular, the Examiner contends that "there is no support in the specification as filed for ATCC Deposit Number 97132," and that "'97132' should be '97165.'" (*See* Paper No. 21, Page 7.)

In response, Applicants thank the Examiner for pointing out the obvious typographical error in claims 96-105 and 123-136. Applicants have canceled claims 96-105 and 123-136, thereby obviating any rejection of these claims. Applicants further note that the correct ATCC Deposit Number, "97165," is recited in the claims added by the present amendment. Accordingly, Applicants submit that the pending claims fully meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

VI. Rejections of the Claims under 35 U.S.C. §112, Second Paragraph.

The Examiner has rejected claims 94, 104, 111, 121 and 135 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. (*See* Paper No. 21, Pages 7-8.) In particular, the Examiner contends that the preambles of these claims are directed to a composition, whereas the remainder of the claims are directed to a single compound (protein).

Applicants have canceled claims 94, 104, 111, 121 and 135, thereby obviating any rejection of these claims. Applicants assert that the claims added by the present amendment do not contain the language objected to by the Examiner. Accordingly, Applicants submit that the pending claims fully meet the requirements of 35 U.S.C. § 112, second paragraph, and respectfully request that the Examiner's rejection of the claims under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

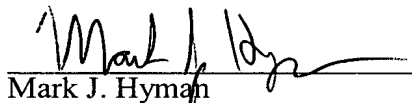
Conclusion

Entry of the above amendment is respectfully solicited. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above or in the Petition for an Extension of Time submitted concurrently herewith, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: March 9, 2001



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Enclosures

VIA HAND DELIVERY MARCH 9, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **COLEMAN et al.**

Application Serial No.: 08/972,301 Art Unit: 1646

Filed: November 18, 1997 Examiner: Kemmerer, E.

For: **Endothelial Monocyte Activating Polypeptide III** Attorney Docket No.: PF206D1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at page 1 after the title, added in the preliminary amendment filed December 3, 1999, has been amended as follows:

This application is a Divisional of and claims priority under 35 U.S.C. § 120 to U.S. Application No. 08/483,534, filed June 7, 1995 (now U.S. Patent No. 6,013,483, issued on January 11, 2000), which is hereby incorporated herein by reference in its entirety. ~~This is a Continuation Application of Serial No. 08/972,301, filed November 18, 1997, which is a divisional of Application Serial No. 08/483,534, filed June 2, 1995.~~

In the Claims:

Claims 90 to 136 have been canceled.